

REMARKS/ARGUMENTS

Claims 7-26 and 30-32 are pending. Claim 7 has been amended to further limit the R<sup>1</sup>, R<sup>2</sup> and R<sup>3</sup> substituents in formula (1). The definition of the second allyl compound finds support in original Claim 3 and on page 15 of the specification and that for the oxygen nucleophilic agent on pages 14, line 18-*et seq.* of the specification. Other minor editorial revisions have been made to some claims, e.g., in Claims 16 and 18-20, changing "(I)" to "(1)" and revising Claims 24 and 30 to further limit the invention. Accordingly, the Applicants do not believe that any new matter has been introduced.

The Applicants thank Examiner Keys for the courteous and helpful interview of June 15, 2006. Approaches to addressing the new matter and prior art rejections were discussed. The Applicants pointed out that Tables 1, 2 and 3 exemplify processes where the oxygen nucleophilic agent and the monodentite phosphite compound are not the same. To help address the prior art rejections based on Woo and Trost (which use carbon nucleophiles), the Applicants were encouraged to point out how carbon and oxygen nucleophiles differ. The superior results obtained by the claimed process were discussed. The Examiner indicated that the examples in the specification refer to phosphites substituted at R1, R2 and R3 with short alkyl, such as isopropyl and ethyl. It was suggested that the Applicants provide examples of other substitutents, such as alkenyl or alkynyl, or cyclic substituents, to further support the scope of these results.

Objection

Claim 15 was objected to as containing a spelling error. This objection is now moot.

Rejection—35 U.S.C. §112, first paragraph

Claims 7-9, 14, 16, 18 and 22 were rejected under 35 U.S.C. 112, first paragraph as lacking adequate description and raising the issue of new matter. This rejection is moot in view of the revision of independent Claim 7.

With respect to the requirement that the oxygen nucleophilic agent and monodentite phosphite differ, the specification exemplifies processes where the oxygen nucleophile and monodentite phosphite are different compounds, see Tables 1, 2 and 3 and Examples 1 and 2 starting on page 59, line 5. The phrase containing “cyclic structure containing oxygen” has been dropped to simplify the claim and the language “in which A is a hydrogen atom or an organic group. . .” finds descriptive support in original Claim 3 and on page 15, line 6 *et seq.* Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §112, second paragraph

Claims 7-16, 18-26 and 30-32 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite. This rejection is moot in view of the amendments above.

Rejection—35 U.S.C. §102

Claims 7-9, 14, 16, 18 and 22 were rejected under 35 U.S.C. 102(b) as being anticipated by Pachamuthu et al., Tetrahedron Letts. 39:5339. This reference does not anticipate the present claims, because the reaction mechanisms differ between Claim 7 and the Pachamuthu process. In Pachamuthu, the X and a hydrogen atom are exchanged through Pd-H (see schemes 1 and 2), but in the present invention, X and Nu are exchanged (see page 2 of the specification). Moreover, in Pachamuthu the second allyl compound is Compound 2 (page 5440, Scheme 1), which does not fall within the present definition of the second allyl compound in independent Claim 7. Accordingly, this rejection may now be withdrawn.

Rejections—35 U.S.C. §102

Claims 7-9, 14, 18, 22, 24, and 30-32 were rejected under 35 U.S.C. 102(b) as being anticipated by Woo et al., U.S. Patent No. 4,567,005. Claims 7-9, 11, 14, 15, 18, 22-24, and 30-32 were rejected under 35 U.S.C. 102(b) as being anticipated by Trost et al., U.S. Patent No. 4,051,157.

Woo or Trost does not anticipate the present invention because it is directed to a process involving a carbon nucleophile, while the invention is directed to a process which uses an oxygen nucleophile. The difference between a carbon and oxygen nucleophile is that the molecular structures of the formed products are fundamentally different. In a reaction between an allyl compound and a carbon nucleophile, carbon-carbon double bonds are formed. On the contrary, in a reaction between an allyl compound and an oxygen nucleophile, carbon-oxygen bonds are formed. Accordingly, the structures of the products formed by the prior art process and that of the invention are fundamentally different from one another.

When two elements, i.e., carbon and oxygen, are compared, carbon has a larger electronegativity. Thus, oxygen nucleophiles are relatively “hard” nucleophiles, whereas carbon nucleophiles by comparison are “soft”. According to the hard-soft-acid-base theory, the soft nucleophiles exhibit a good reactivity with other soft electrophiles (see e.g., Reference Document 1, attached).

In the present invention, it has been found that the reactivity of a catalyst can be increased by using a phosphite having a specific structure, and an allyl-Pd complex as a soft electrophile can be efficiently reacted with oxygen nucleophiles as hard nucleophiles. This finding overturns the common technical knowledge of those skilled in the art as of the filing date of this application.

Even if Woo or Trost did suggest that a phosphite compounds could be applied to synthesize an allyl compound of the invention, one with ordinary skill in the art would not have inferred that a catalyst using a specific phosphite compound would exhibit superior reactivity with oxygen nucleophiles. Accordingly, these rejections may now be withdrawn.

Rejection—35 U.S.C. §103

Claims 7 and 23 were rejected under 35 U.S.C. 103(a) as being unpatentable over Woo et al., U.S. Patent No. 4,567,005.

The Applicants respectfully request that this rejection be withdrawn in view of the remarks above, e.g., Woo does not disclose the oxygen nucleophiles of the invention, but is directed to carbon nucleophiles.

Moreover, Woo does not disclose or suggest all the elements of the invention, namely a palladium catalyst, and there is no suggestion in Woo that different transition metals exhibit similar catalytic properties.

Rejection—35 U.S.C. §103

Claims 7-10, 16, 18, 22, 24, 25 and 30-32 were rejected under 35 U.S.C. 103(a) as being anticipated by Arend et al., U.S. Patent No. 4,017,564. The Applicants response is reiterated below.

Response to remarks on page 7 of the Official Action: Claim 7 requires that the monodentite phosphite and the oxygen nucleophilic agent are different compounds. Even if the trialkyl phosphite in Arend exerts catalytic activity, it would still be the same as the oxygen nucleophilic agent and thus fall outside of Claim 7 (see side-by-side comparison below).

Response to Rejection: This rejection is moot in view of the amendment of Claim 7 which requires that the oxygen nucleophilic agent is different from the monodentate phosphite catalyst. A comparison of the process of Claim 7 and the process of Arendt is shown below:

<u>Claim 7:</u>	<u>Arendt</u>
<u>Substrates/Catalyst</u>	
First allyl compound	allyl chloride or methallyl chloride
Oxygen nucleophilic agent	trialkyl phosphite
Monodentate phosphite (catalyst)	trialkyl phosphite
Transition metal (catalyst)	Ni or Co
<u>Product:</u>	
Second allyl compound	allyl or methallyl phosphonic acid ester

Claim 7 requires that the monodentate phosphite and the oxygen nucleophilic agent be different. However, in Arendt the oxygen nucleophilic agent and the monodentate phosphite are the same. Moreover, Arendt discloses the trialkyl phosphite as a substrate and not a catalyst. A catalyst accelerates a reaction, but does not participate in the reaction. Accordingly, the Applicants respectfully request that this rejection be withdrawn.

Rejection—35 U.S.C. §103

Claims 7-26 and 30-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Kurtz et al., U.S. Patent No. 3,755,451 alone or in view of Bryant et al., U.S. Patent No. 3,534,088 or Hefner, Jr., U.S. Patent 4,613,703.

The cited prior art does not disclose or suggest the present invention, which uses a phosphite of formula (1), nor provide a reasonable expectation of success for the superior results obtained by the present invention.

While Kurtz, col. 7, lines 38-41 and col. 8, lines 43-*et seq.* disclose a wide variety of catalyst modifiers, including various phosphines and phosphites, it provides no suggestion to specifically select phosphites of formula (1). As shown in Tables 1 and 2 on pages 60 and 62 of the specification, the selection of phosphites of formula (1) provides a significantly superior process compared to use of phosphines or other phosphites.

Bryant also does not provide any such suggestion or reasonable expectation of success for the claimed process.

Hefner, Jr. et al. disclose a quaternary salt having the formula  $Z^+(R^1)(R^2)(R^3)(R^4)A^-$ . Claim 7 requires a monodentate phosphite compound having formula (1):  $P(OR^1)(OR^2)(OR^3)$ , wherein  $R^1$ ,  $R^2$  and  $R^3$  are independently a linear or branched alkyl group which may have a substituent. Thus, Hefner, Jr. is non-analogous art, because it does not disclose the catalyst of formula (1). Accordingly, the Applicants respectfully request that this rejection be withdrawn.

CONCLUSION

In view of the above amendments and remarks, the Applicants respectfully submit that this application is now in condition for allowance. Early notification to that effect is earnestly solicited.

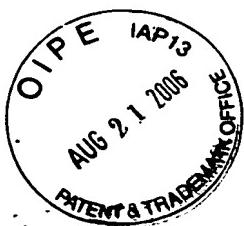
Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,  
MAIER & NEUSTADT, P.C.  
Norman F. Oblon

Customer Number  
**22850**

Tel: (703) 413-3000  
Fax: (703) 413 -2220  
(OSMMN 06/04)  
TMC:aif

  
Thomas M. Cunningham  
Attorney of Record  
Registration No. 45,394



# *Palladium Reagents and Catalysts*

## *Innovations in Organic Synthesis*

JIRO TSUJI

*Okayama University of Science, Okayama, Japan*



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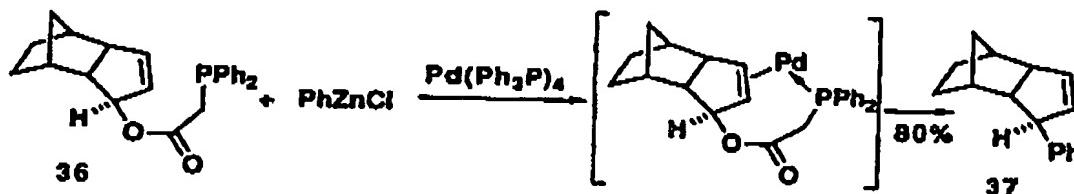
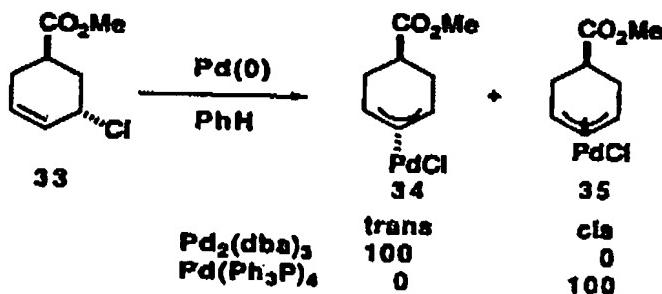
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## Reactions of Allylic Compounds

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In some cases,  $\pi$ -allylpalladium complex formation by retention (*syn* attack) has been observed. The reaction of the cyclic allylic chloride 33 with Pd(0) affords the  $\pi$ -allylpalladium chlorides 34 and 35 by retention or inversion depending on the solvents and Pd species. For example, retention is observed in benzene, THF, or dichloromethane with  $Pd_2(dbu)_3$ . However, the complex formation proceeds by inversion in these solvents with  $Pd(Ph_3P)_4$ , whereas in MeCN and DMSO it is always inversion[33]. The *syn* attack in this case may be due to coordination of Pd to chlorine in 33, because Pd is halophilic. The definite *syn* attack in complex formation has been observed using stereochemically biased substrates. The reaction of the *exo*-allylic diphenylphosphino-acetate 36 with phenylzinc proceeds smoothly to give 37. The reaction can be explained by complex formation by a *syn* mechanism[31]. However, these *syn* attacks are exceptional, and normally *anti* attack dominates.

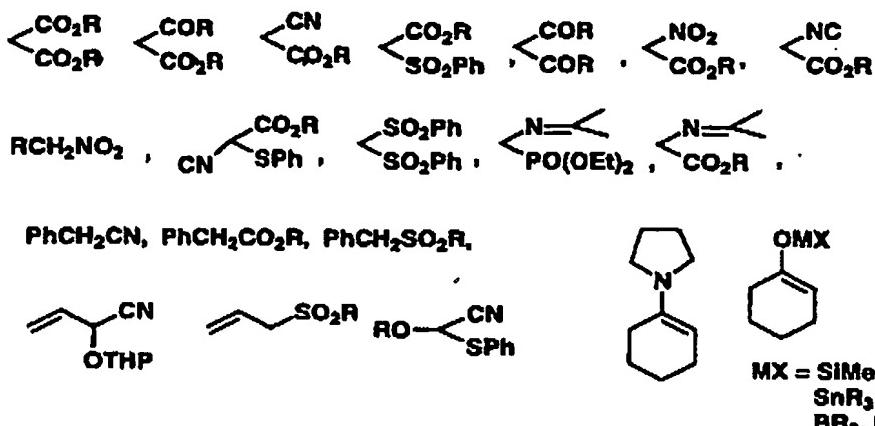


## 2.2.2 Allylation of Soft Carbon Nucleophiles

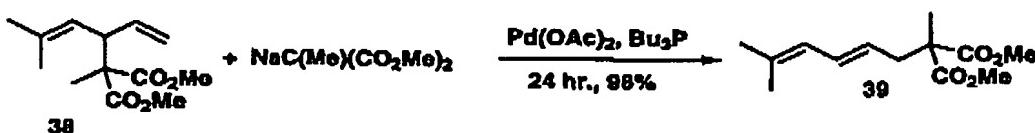
$\pi$ -Allylpalladium cations can be regarded as 'soft' electrophiles, and react most smoothly with 'soft' nucleophiles. Compounds which have the electron-withdrawing groups (EWGs) shown are allylated. Typically, active methylene or methine compounds which are activated by two EWGs, such as carbonyl, sulfonyl, cyano, and nitro, are allylated by the Pd-catalyzed reactions of allylic compounds. Aryl groups (arylacetonitrile, phenylacetate)[14], olefinic bonds ( $\beta,\gamma$ -unsaturated sulfones, ketones)[11], and imino groups[34–36], are also activating groups. Methoxy(phenylthio)acetonitrile as a precursor of an ester is also reactive for allylation[37]. Nitroalkanes alone are allylated without being activated by other EWGs[38,39]. Both stoichiometric and catalytic allylations of nucleophiles via  $\pi$ -allylpalladium intermediates are called Tsuji–Trost reactions.

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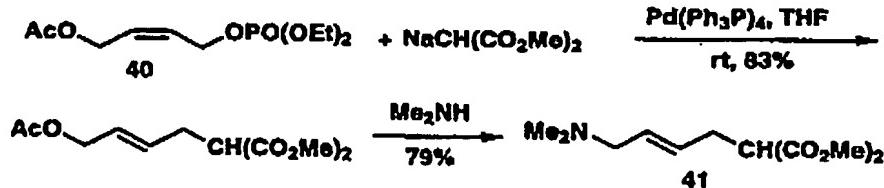
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*Catalytic Reactions with Pd(0) and Pd(II)*

Interestingly, the allylation of a stabilized carbon nucleophile has been found to be reversible. Complete isomerization of dimethyl methylmalonate, involving bis-allylic C—C bond cleavage, from a secondary carbon 38 to a primary carbon 39 was observed by treatment with a Pd catalyst for 24 h. The C—C bond cleavage of a monoallylic system proceeds slowly[40].



**2.2.2.1 Allylation under basic conditions.** Allylation can be carried out under basic conditions with allylic acetates and phosphates, and under neutral conditions with carbonates and vinyloxiranes. The allylations under neutral conditions are treated separately in Section 2.2.2.2 from those under basic conditions. However, in some cases, allylations of the same substrates are carried out under both basic and neutral conditions to give similar results. These reactions are treated together in this section for convenience. Allylic acetates are widely used for Pd-catalyzed allylation in the presence of bases; tertiary amines or NaH are commonly used[6,7,41]. As a base, basic alumina or KF on alumina is conveniently used, because it is easy to remove by filtration after the reaction[42]. Allyl phosphates are more reactive than acetates. The allylation with 40 proceeds stepwise. At first allylic phosphate reacts with malonate and then allylic acetate reacts with amine to give 41[43].



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